

REMARKS

Introductory Comments

1-16 and 38-41 were examined in the Office Action under reply and were variously rejected under (1) 35 U.S.C. §112, second paragraph; and (2) 35 U.S.C. §103(a). These rejections are traversed and believed to be overcome for reasons discussed below.

Restriction Requirement

Applicants affirm the election without traverse to prosecute the claims of Group I, claims 1-16 and 38-41, directed to compositions and kits comprising semiconductor nanoparticle complexes. Applicants request that claims 17-37, drawn to methods of using the complexes, be rejoined, per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products. Applicants request that claims 17-37 be rejoined and examined upon allowance of any of the claims of Group I.

Overview of the Amendments

Claims 1, 3, 4, 12 and 38-41 have been amended to recite the invention with greater particularity. In this regard, claims 1 and 12 now recite that the semiconductor nanoparticle is "bound to" the cationic polymer. As is readily apparent, the nanoparticle may be non-covalently bound to the cationic polymer, as is the case with the HIV-tat sequence used in Example 1 (see, page 87, lines 9-13 of the application). Alternatively, the semiconductor nanoparticle can be covalently bound to the cationic polymer. In fact, many HIV-tat sequences are used in this configuration. See, e.g., U.S. Patent No. 5,652,122 to Frankel et al., cited by the Examiner. The semiconductor nanoparticle can also form an ionic bond with the polymer, or even be linked to the cationic polymer via a spacer or linker (see, e.g., page 34, lines 3-23 of the application).

Claim 1 has also been amended to incorporate the recitations from now canceled

claim 2. Claims 3 and 4 have been amended to correct typographical errors. Claim 3 has also been amended to depend from claim 1 rather than canceled claim 2. Claims 38-41 have been amended to correct antecedent basis, as requested by the Examiner.

The amendments are made solely to expedite prosecution, for reasons unrelated to patentability, and do not constitute an acknowledgment that the Examiner's position is correct. In view of the foregoing amendments and following remarks, applicants submit that the application is in condition for allowance.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1-16 and 38-41 were rejected as indefinite. In particular, the Office objected to the term "associated with" in claims 1 and 12 and the term "encoded cell" in claims 38-41. These terms have been eliminated from the claims, as explained above. Thus, these bases for rejection have been overcome and withdrawal thereof is respectfully requested.

Rejections Under 35 U.S.C. §103(a)

Claims 1-7, 10-13, 16, 38, 39 and 41 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,306,610 to Bawendi et al. ("Bawendi") in view of U.S. Patent No. 6,306,993 to Rothbard et al. ("Rothbard"). However, applicants do not agree that the cited combination renders the claims obvious.

To support an obviousness rejection under 35 U.S.C. § 103, "all the claim limitations must be taught or suggested by the prior art." MPEP §2143.03. In addition, "the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure." MPEP §706.02. Applicants submit that the cited references do not disclose or suggest all the limitations of the present invention. Thus, a *prima facie* case of obviousness has not been presented by the Office, and the cited combination is based on impermissible hindsight reconstruction.

As acknowledged by the Examiner, Bawendi does not teach or suggest a semiconductor nanoparticle associated with a cationic polymer capable of enhancing the

transport of the nanoparticle across a biological membrane as claimed, and does not suggest a tat peptide from the protein transduction domain of the HIV tat protein. Nor does Bawendi teach or suggest a kit comprising such complexes. Therefore, Bawendi fails to provide any motivation for such a complex.

The reference of Rothbard fails to cure the deficiencies of Bawendi. Rothbard pertains to the transport of drugs and macromolecules across biological membranes. The goal of Rothbard is to promote transport of a biological agent across a membrane in order to achieve a therapeutic effect. Rothbard is not attempting to enhance the transport of a label, let alone a semiconductor nanocrystal, across a biological membrane. In fact, the molecules transported by Rothbard are not analogous to semiconductor nanocrystals in any way. Specifically, semiconductor nanocrystals are colloidal suspensions as opposed to organic soluble molecules and macromolecules as described by Rothbard. Indeed, semiconductor nanocrystals are considered to be a physical form somewhere between molecular and bulk phase materials. There is absolutely no reason to believe that carrier peptides employed to transport organic molecules across biological membranes would also successfully transport inorganic nanocrystals across biological membranes.

Moreover, semiconductor nanocrystals comprising a shell and core, such as claimed in dependent claims 3-7, 12-16 and 39-41, are complex multilayer structures that have an average composition, analogous to a polymer. These complex multilayer structures are not the same as the molecules transported by Rothbard and there is no suggestion in Rothbard to use a transport polymer with such a structure. The combination of Bawendi with Rothbard provides no information regarding the ability of cationic polymers to enhance the transport of crystalline particles, such as semiconductor nanocrystals, across biological membranes.

Applicants submit that no motivation to combine the teachings of Bawendi and Rothbard can be found in the references themselves. Thus, the references do not disclose or suggest all the limitations of the present invention, and the Examiner has not met the burden of establishing a *prima facie* case of obviousness. In the absence of some teaching or suggestion in the cited references concerning the precisely claimed semiconductor nanocrystal/cationic

polymer complexes, as described in the present application, the Examiner has presented no more than an improper hindsight reconstruction of the present invention. As stated by the Court of Appeals for the Federal Circuit *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988): “One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.”

Therefore, the Office has not met the requirements for a *prima facie* showing of obviousness under 35 U.S.C. § 103. For at least the above reasons, withdrawal of the above rejection under 35 U.S.C. § 103(a) is respectfully requested.

Claims 8, 9, 14, 15 and 40 were rejected under 35 U.S.C. §103(a) over the combination of Bawendi in view of U.S. Patent No. 5,652,122 to Frankel et al. (“Frankel”). Bawendi is applied as above. Frankel is said to teach the “intracellular delivery of cargo molecules by the use of transport polypeptides which comprise HIV tat protein or one or more portions thereof and which are covalently attached to the cargo molecules.” Office Action, page 7. However, applicants respectfully submit that the claims are patentable over the combination of Bawendi and Frankel.

In particular, the Office correctly notes Bawendi fails to teach the use of a tat peptide from the protein transduction domain of the HIV tat protein and a kit including the same. As explained above, Bawendi does not provide the motivation to make such a complex. Frankel does not supply the missing link. Frankel, like Rothbard above, pertains to the delivery of nucleic acid and protein molecules, not crystalline particles, as claimed. As explained above, the properties of such molecules are very different than crystalline particles. Thus, the combination of Bawendi with Frankel is not believed to render the claimed invention obvious and withdrawal of this basis for rejection is respectfully requested.

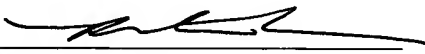
CONCLUSION

Applicants respectfully submit the claims define a patentable invention. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters which may be resolved by a telephone interview, the Examiner is encouraged to contact the undersigned by telephone at 650-493-3400.

Respectfully submitted,

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